



SEQUENCE LISTING

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TECH CENTER 1600/2900

<110> ANDERSON, Dirk, M.
GALIBERT, Laurent, J.

<120> METHOD OF INHIBITING OSTEOCLAST ACTIVITY

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<140> 09/705,985

<141> 2000-11-03

<150> PCT/US99/10588

<151> 1999-05-13

<150> 60/085,487

<151> 1998-05-14

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<150> 60/059,978

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<160> 8

<170> PatentIn version 3.1

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<222> (39)..(1886)

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Arg Leu Gln Val Ala Leu Gln Ile Ala Pro Pro Cys Thr Ser Glu Lys
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Tyr Met Ser Ser Lys Cys Thr Thr Thr Ser Asp Ser Val Cys Leu Pro	
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Cys Gly Pro Asp Glu Tyr Leu Asp Ser Trp Asn Glu Glu Asp Lys Cys	
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Cys Lys Pro Cys Leu Ala Gly Tyr Phe Ser Asp Ala Phe Ser Ser Thr	
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Glu His His Gly Thr Glu Lys Ser Asp Ala Val Cys Ser Ser Ser Leu	
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Thr	Cys	Val	Gly	Gly	Gly	Pro	Tyr	Ala	Gln	Gly	Glu	Asp	Ala	Arg	Met	
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Gln	Leu	Leu	Phe	Leu	Thr	Glu	Pro	Gly	Ser	Lys	Ser	Thr	Pro	Pro	Phe	
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Pro	Leu	Cys	Arg	Thr	Asp	Trp	Thr	Pro	Met	Ser	Ser	Glu	Asn	Tyr	Leu	
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Ser	Pro	Asn	Trp	Ala	Asp	Val	Cys	Thr	Gly	Cys	Arg	Asn	Pro	Pro	Gly	
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Glu	Asp	Cys	Glu	Pro	Leu	Val	Gly	Ser	Pro	Lys	Arg	Gly	Pro	Leu	Pro	
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Gln	Cys	Ala	Tyr	Gly	Met	Gly	Leu	Pro	Pro	Glu	Glu	Glu	Ala	Ser	Arg	
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Thr	Glu	Ala	Arg	Asp	Gln	Pro	Glu	Asp	Gly	Ala	Asp	Gly	Arg	Leu	Pro	
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Lys Cys Glu Pro Gly Lys Tyr Met Ser Ser Lys Cys Thr Thr Thr Ser
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Asp Ser Val Cys Leu Pro Cys Gly Pro Asp Glu Tyr Leu Asp Ser Trp
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Asn Glu Glu Asp Lys Cys Leu Leu His Lys Val Cys Asp Thr Gly Lys
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Ala Leu Val Ala Val Val Ala Gly Asn Ser Thr Thr Pro Arg Arg Cys
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Ala Cys Thr Ala Gly Tyr His Trp Ser Gln Asp Cys Glu Cys Cys Arg
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Val Cys Ser Ser Ser Leu Pro Ala Arg Lys Pro Pro Asn Glu Pro His
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Val Tyr Leu Pro Gly Leu Ile Ile Leu Leu Leu Phe Ala Ser Val Ala
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Lys Ser Thr Pro Pro Phe Ser Glu Pro Leu Glu Val Gly Glu Asn Asp
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His Trp Ala Ala Ser Pro Ser Pro Asn Trp Ala Asp Val Cys Thr Gly

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440

445

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Ser Ser Pro Gly Gly Gln Ser Pro Ala Ser Gly Asn Val Thr Gly Asn
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Asp Gly Val	Glu Val His	Asn Ala Lys	Thr Lys Pro Arg Glu Glu Gln
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Tyr Asn Ser	Thr Tyr Arg	Val Val Ser	Val Leu Thr Val Leu His Gln
	85	90	95
Asp Trp Leu	Asn Gly Lys	Asp Tyr Lys	Cys Lys Val Ser Asn Lys Ala
	100	105	110
Leu Pro Ala	Pro Met Gln	Lys Thr Ile	Ser Lys Ala Lys Gly Gln Pro
	115	120	125
Arg Glu Pro	Gln Val Tyr	Thr Leu Pro	Pro Ser Arg Asp Glu Leu Thr
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Lys Asn Gln	Val Ser Leu	Thr Cys Leu	Val Lys Gly Phe Tyr Pro Arg
145	150		155 160
His Ile Ala	Val Glu Trp	Glu Ser Asn	Gly Gln Pro Glu Asn Asn Tyr
	165	170	175
Lys Thr Thr	Pro Pro Val	Leu Asp Ser	Asp Gly Ser Phe Phe Leu Tyr
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Ser Lys Leu	Thr Val Asp	Lys Ser Arg	Trp Gln Gln Gly Asn Val Phe
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Ala Leu Cys Val Leu Leu Val Pro Leu Gln Val Thr Leu Gln Val Thr
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cct cca tgc acc cag gag agg cat tat gag cat ctc gga cgg tgt tgc      144
Pro Pro Cys Thr Gln Glu Arg His Tyr Glu His Leu Gly Arg Cys Cys
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agc aga tgc gaa cca gga aag tac ctg tcc tct aag tgc act cct acc      192
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Ser Asp Ser Val Cys Leu Pro Cys Gly Pro Asp Glu Tyr Leu Asp Thr
65                               70                               75          80

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Trp Asn Glu Glu Asp Lys Cys Leu Leu His Lys Val Cys Asp Ala Gly
                85                               90          95

aag gcc ctg gtg gcg gtg gat cct ggc aac cac acg gcc ccg cgt cgc      336
Lys Ala Leu Val Ala Val Asp Pro Gly Asn His Thr Ala Pro Arg Arg
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Cys Ala Cys Thr Ala Gly Tyr His Trp Asn Ser Asp Cys Glu Cys Cys
                115                              120          125

cgc agg aac acg gag tgt gca cct ggc ttc gga gct cag cat ccc ttg      432
Arg Arg Asn Thr Glu Cys Ala Pro Gly Phe Gly Ala Gln His Pro Leu
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145                              150                              155          160

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Ser Asp Val Phe Ser Ser Thr Asp Lys Cys Lys Pro Trp Thr Asn Cys
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acc ctc ctt gga aag cta gaa gca cac cag ggg aca acg gaa tca gat      576
Thr Leu Leu Gly Lys Leu Glu Ala His Gln Gly Thr Thr Glu Ser Asp
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Val Val Cys Ser Ser Ser Met Thr Leu Arg Arg Pro Pro Lys Glu Ala
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225 230 235 240	
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Lys Ala Leu Thr Ala Asn Leu Trp Asn Trp Val Asn Asp Ala Cys Ser	
245 250 255	
agt cta agt gga aat aag gag tcc tca ggg gac cgt tgt gct ggt tcc	816
Ser Leu Ser Gly Asn Lys Glu Ser Ser Gly Asp Arg Cys Ala Gly Ser	
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cac tcg gca acc tcc agt cag caa gaa gtg tgt gaa ggt atc tta cta	864
His Ser Ala Thr Ser Ser Gln Gln Glu Val Cys Glu Gly Ile Leu Leu	
275 280 285	
atg act cgg gag gag aag atg gtt cca gaa gac ggt gct gga gtc tgt	912
Met Thr Arg Glu Glu Lys Met Val Pro Glu Asp Gly Ala Gly Val Cys	
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Gly Pro Val Cys Ala Ala Gly Gly Pro Trp Ala Glu Val Arg Asp Ser	
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Pro Arg Phe Pro Asp Val Cys Ala Thr Gly Ala Gly Leu Gln Glu Gln	
580 585 590	
ggg gca ccc ccg cag aag gac ggg aca tcg ccg ccg gtg cag gag cag	1824
Gly Ala Pro Arg Gln Lys Asp Gly Thr Ser Arg Pro Val Gln Glu Gln	
595 600 605	
ggg ggc gcg cag act tca ctc cat acc cag ggg tcc gga caa tgt gca	1872
Gly Gly Ala Gln Thr Ser Leu His Thr Gln Gly Ser Gly Gln Cys Ala	
610 615 620	
gaa tga	1878
Glu	
625	

<210> 5
 <211> 625
 <212> PRT
 <213> Murine

<400> 5

Met Ala Pro Arg Ala Arg Arg Arg Arg Gln Leu Pro Ala Pro Leu Leu
1 5 10 15

Ala Leu Cys Val Leu Leu Val Pro Leu Gln Val Thr Leu Gln Val Thr

20

25

30

Pro Pro Cys Thr Gln Glu Arg His Tyr Glu His Leu Gly Arg Cys Cys
 35 40 45

Ser Arg Cys Glu Pro Gly Lys Tyr Leu Ser Ser Lys Cys Thr Pro Thr
 50 55 60

Ser Asp Ser Val Cys Leu Pro Cys Gly Pro Asp Glu Tyr Leu Asp Thr
 65 70 75 80

Trp Asn Glu Glu Asp Lys Cys Leu Leu His Lys Val Cys Asp Ala Gly
 85 90 95

Lys Ala Leu Val Ala Val Asp Pro Gly Asn His Thr Ala Pro Arg Arg
 100 105 110

Cys Ala Cys Thr Ala Gly Tyr His Trp Asn Ser Asp Cys Glu Cys Cys
 115 120 125

Arg Arg Asn Thr Glu Cys Ala Pro Gly Phe Gly Ala Gln His Pro Leu
 130 135 140

Gln Leu Asn Lys Asp Thr Val Cys Thr Pro Cys Leu Leu Gly Phe Phe
 145 150 155 160

Ser Asp Val Phe Ser Ser Thr Asp Lys Cys Lys Pro Trp Thr Asn Cys
 165 170 175

Thr Leu Leu Gly Lys Leu Glu Ala His Gln Gly Thr Thr Glu Ser Asp
 180 185 190

Val Val Cys Ser Ser Ser Met Thr Leu Arg Arg Pro Pro Lys Glu Ala
 195 200 205

Gln Ala Tyr Leu Pro Ser Leu Ile Val Leu Leu Leu Phe Ile Ser Val
 210 215 220

Val Val Val Ala Ala Ile Ile Phe Gly Val Tyr Tyr Arg Lys Gly Gly
 225 230 235 240

Lys Ala Leu Thr Ala Asn Leu Trp Asn Trp Val Asn Asp Ala Cys Ser
 245 250 255

Ser Leu Ser Gly Asn Lys Glu Ser Ser Gly Asp Arg Cys Ala Gly Ser
 260 265 270

His Ser Ala Thr Ser Ser Gln Gln Glu Val Cys Glu Gly Ile Leu Leu
 275 280 285

Met Thr Arg Glu Glu Lys Met Val Pro Glu Asp Gly Ala Gly Val Cys
 290 295 300

Gly Pro Val Cys Ala Ala Gly Gly Pro Trp Ala Glu Val Arg Asp Ser
 305 310 315 320

Arg Thr Phe Thr Leu Val Ser Glu Val Glu Thr Gln Gly Asp Leu Ser
 325 330 335

Arg Lys Ile Pro Thr Glu Asp Glu Tyr Thr Asp Arg Pro Ser Gln Pro
 340 345 350

Ser Thr Gly Ser Leu Leu Leu Ile Gln Gln Gly Ser Lys Ser Ile Pro
 355 360 365

Pro Phe Gln Glu Pro Leu Glu Val Gly Glu Asn Asp Ser Leu Ser Gln
 370 375 380

Cys Phe Thr Gly Thr Glu Ser Thr Val Asp Ser Glu Gly Cys Asp Phe
 385 390 395 400

Thr Glu Pro Pro Ser Arg Thr Asp Ser Met Pro Val Ser Pro Glu Lys
 405 410 415

His Leu Thr Lys Glu Ile Glu Gly Asp Ser Cys Leu Pro Trp Val Val
 420 425 430

Ser Ser Asn Ser Thr Asp Gly Tyr Thr Gly Ser Gly Asn Thr Pro Gly
 435 440 445

Glu Asp His Glu Pro Phe Pro Gly Ser Leu Lys Cys Gly Pro Leu Pro
 450 455 460

Gln Cys Ala Tyr Ser Met Gly Phe Pro Ser Glu Ala Ala Ala Ser Met
 465 470 475 480

Ala Glu Ala Gly Val Arg Pro Gln Asp Arg Ala Asp Glu Arg Gly Ala
 485 490 495

Ser Gly Ser Gly Ser Ser Pro Ser Asp Gln Pro Pro Ala Ser Gly Asn
 500 505 510

Val Thr Gly Asn Ser Asn Ser Thr Phe Ile Ser Ser Gly Gln Val Met
 515 520 525

Asn Phe Lys Gly Asp Ile Ile Val Val Tyr Val Ser Gln Thr Ser Gln
 530 535 540

Glu Gly Pro Gly Ser Ala Glu Pro Glu Ser Glu Pro Val Gly Arg Pro
 545 550 555 560

Val Gln Glu Glu Thr Leu Ala His Arg Asp Ser Phe Ala Gly Thr Ala
 565 570 575

Pro Arg Phe Pro Asp Val Cys Ala Thr Gly Ala Gly Leu Gln Glu Gln
 580 585 590

Gly Ala Pro Arg Gln Lys Asp Gly Thr Ser Arg Pro Val Gln Glu Gln
 595 600 605

Gly Gly Ala Gln Thr Ser Leu His Thr Gln Gly Ser Gly Gln Cys Ala
 610 615 620

Glu
 625

<210> 6
 <211> 33
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Murine

<400> 6

Arg Met Lys Gln Ile Glu Asp Lys Ile Glu Glu Ile Leu Ser Lys Ile
 1 5 10 15

Tyr His Ile Glu Asn Glu Ile Ala Arg Ile Lys Lys Leu Ile Gly Glu
 20 25 30

Arg

<210> 7
 <211> 954
 <212> DNA
 <213> Homo sapiens;

<220>

<221> CDS
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 <223>

<400> 7

atg cgc cgc gcc agc aga gac tac acc aag tac ctg cgt ggc tcg gag	48
Met Arg Arg Ala Ser Arg Asp Tyr Thr Lys Tyr Leu Arg Gly Ser Glu	
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gag atg ggc ggc ggc ccc gga gcc ccg cac gag ggc ccc ctg cac gcc	96
Glu Met Gly Gly Gly Pro Gly Ala Pro His Glu Gly Pro Leu His Ala	
20 25 30	
ccg ccg ccg cct gcg ccg cac cag ccc ccc gcc gcc tcc cgc tcc atg	144
Pro Pro Pro Pro Ala Pro His Gln Pro Pro Ala Ala Ser Arg Ser Met	
35 40 45	
ttc gtg gcc ctc ctg ggg ctg ggg ctg ggc cag gtt gtc tgc agc gtc	192
Phe Val Ala Leu Leu Gly Leu Gly Leu Gly Gln Val Val Cys Ser Val	
50 55 60	
gcc ctg ttc ttc tat ttc aga gcg cag atg gat cct aat aga ata tca	240
Ala Leu Phe Phe Tyr Phe Arg Ala Gln Met Asp Pro Asn Arg Ile Ser	
65 70 75 80	
gaa gat ggc act cac tgc att tat aga att ttg aga ctc cat gaa aat	288
Glu Asp Gly Thr His Cys Ile Tyr Arg Ile Leu Arg Leu His Glu Asn	
85 90 95	
gca gat ttt caa gac aca act ctg gag agt caa gat aca aaa tta ata	336
Ala Asp Phe Gln Asp Thr Thr Leu Glu Ser Gln Asp Thr Lys Leu Ile	
100 105 110	
cct gat tca tgt agg aga att aaa cag gcc ttt caa gga gct gtg caa	384
Pro Asp Ser Cys Arg Arg Ile Lys Gln Ala Phe Gln Gly Ala Val Gln	
115 120 125	
aag gaa tta caa cat atc gtt gga tca cag cac atc aga gca gag aaa	432
Lys Glu Leu Gln His Ile Val Gly Ser Gln His Ile Arg Ala Glu Lys	
130 135 140	
gcg atg gtg gat ggc tca tgg tta gat ctg gcc aag agg agc aag ctt	480
Ala Met Val Asp Gly Ser Trp Leu Asp Leu Ala Lys Arg Ser Lys Leu	
145 150 155 160	
gaa gct cag cct ttt gct cat ctc act att aat gcc acc gac atc cca	528
Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Thr Asp Ile Pro	
165 170 175	
tct ggt tcc cat aaa gtg agt ctg tcc tct tgg tac cat gat cgg ggt	576
Ser Gly Ser His Lys Val Ser Leu Ser Ser Trp Tyr His Asp Arg Gly	
180 185 190	
tgg gcc aag atc tcc aac atg act ttt agc aat gga aaa cta ata gtt	624
Trp Ala Lys Ile Ser Asn Met Thr Phe Ser Asn Gly Lys Leu Ile Val	
195 200 205	
aat cag gat ggc ttt tat tac ctg tat gcc aac att tgc ttt cga cat	672
Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His	
210 215 220	

cat gaa act tca gga gac cta gct aca gag tat ctt caa cta atg gtg 720
 His Glu Thr Ser Gly Asp Leu Ala Thr Glu Tyr Leu Gln Leu Met Val
 225 230 235 240

tac gtc act aaa acc agc atc aaa atc cca agt tct cat acc ctg atg 768
 Tyr Val Thr Lys Thr Ser Ile Lys Ile Pro Ser Ser His Thr Leu Met
 245 250 255

aaa gga gga agc acc aag tat tgg tca ggg aat tct gaa ttc cat ttt 816
 Lys Gly Gly Ser Thr Lys Tyr Trp Ser Gly Asn Ser Glu Phe His Phe
 260 265 270

tat tcc ata aac gtt ggt gga ttt ttt aag tta cgg tct gga gag gaa 864
 Tyr Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ser Gly Glu Glu
 275 280 285

atc agc atc gag gtc tcc aac ccc tcc tta ctg gat ccg gat cag gat 912
 Ile Ser Ile Glu Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp
 290 295 300

gca aca tac ttt ggg gct ttt aaa gtt cga gat ata gat tga 954
 Ala Thr Tyr Phe Gly Ala Phe Lys Val Arg Asp Ile Asp
 305 310 315

<210> 8
 <211> 317
 <212> PRT
 <213> Homo sapiens;

<400> 8

Met Arg Arg Ala Ser Arg Asp Tyr Thr Lys Tyr Leu Arg Gly Ser Glu
 1 5 10 15

Glu Met Gly Gly Gly Pro Gly Ala Pro His Glu Gly Pro Leu His Ala
 20 25 30

Pro Pro Pro Pro Ala Pro His Gln Pro Pro Ala Ala Ser Arg Ser Met
 35 40 45

Phe Val Ala Leu Leu Gly Leu Gly Leu Gly Gln Val Val Cys Ser Val
 50 55 60

Ala Leu Phe Phe Tyr Phe Arg Ala Gln Met Asp Pro Asn Arg Ile Ser
 65 70 75 80

Glu Asp Gly Thr His Cys Ile Tyr Arg Ile Leu Arg Leu His Glu Asn
 85 90 95

Ala Asp Phe Gln Asp Thr Thr Leu Glu Ser Gln Asp Thr Lys Leu Ile
 100 105 110

Pro Asp Ser Cys Arg Arg Ile Lys Gln Ala Phe Gln Gly Ala Val Gln
 115 120 125

Lys Glu Leu Gln His Ile Val Gly Ser Gln His Ile Arg Ala Glu Lys
 130 135 140

Ala Met Val Asp Gly Ser Trp Leu Asp Leu Ala Lys Arg Ser Lys Leu
 145 150 155 160

Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Thr Asp Ile Pro
 165 170 175

Ser Gly Ser His Lys Val Ser Leu Ser Ser Trp Tyr His Asp Arg Gly
 180 185 190

Trp Ala Lys Ile Ser Asn Met Thr Phe Ser Asn Gly Lys Leu Ile Val
 195 200 205

Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His
 210 215 220

His Glu Thr Ser Gly Asp Leu Ala Thr Glu Tyr Leu Gln Leu Met Val
 225 230 235 240

Tyr Val Thr Lys Thr Ser Ile Lys Ile Pro Ser Ser His Thr Leu Met
 245 250 255

Lys Gly Gly Ser Thr Lys Tyr Trp Ser Gly Asn Ser Glu Phe His Phe
 260 265 270

Tyr Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ser Gly Glu Glu
 275 280 285

Ile Ser Ile Glu Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp
 290 295 300

Ala Thr Tyr Phe Gly Ala Phe Lys Val Arg Asp Ile Asp
 305 310 315